peculiar to man allows for the learning of language and social habits, and is undoubtedly the result of selection of factors making for delayed adolescence, enabling the more co-operative groups of people to survive.

It is an interesting question whether still closer social co-operation might be achieved by a society that adopted some method of clonal reproduction by which all men were truly brothers. Altruism is an effective evolutionary policy only if it benefits your own genes, and the ants and bees use very special methods to ensure this. Technically such changes begin to look almost possible; whether they are desirable is another matter. We certainly cannot foresee them in the near future, but the possibility of them may remind us that the biggest difference of all between men and animals is in the vast range of techniques of control of life that are now becoming available. We are all familiar with the effects of the techniques of physical science in promoting the industrial revolution and the invention of machines. Perhaps it is still insufficiently realized that biological knowledge is now producing a still greater revolution, namely in the way we manage ourselves. Inevitably the medical profession finds itself in the forefront of this revolution and has to learn to deal with all the new problems that it brings.

This symposium is especially welcome for that reason. I should like to emphasize once more that the problems are those of information and control. We shall collect much information today. We shall probably not have much to say about the problems of how it is to be used for the control of human life. But I hope that we shall not forget that if we are to achieve successful regulation in the future we shall have to be ready to use and to accept control in matters of population and environment. The need for such control should not alarm us, if it is properly based on information and feed-back. After all, it is a natural extension of the regulation by the information of our DNA or by the language and social customs that we inherit from the past.

We should never forget that the continuation of our lives depends every moment on information from the past. We are as we are because of the endowment we receive, particularly from our genes, our language and our social system. Without them we are nothing. Life depends upon regulation, and the opposite of control is death. We should be thankful that we are subject to genetic, linguistic and social systems that allow us a full and developing life, however far it may be from perfection, whatever that may mean.

Let us rejoice in the fact that we live at a time when ever-fresh sources of information abound, and when people are beginning to realize the need for closer and closer co-operation for survival.

Death Squared: The Explosive Growth and Demise of a Mouse Population

by John B Calhoun MD
*(Section on Behavioral Systems,
Laboratory of Brain Evolution & Behavior,
National Institute of Mental Health,
9000 Rockville Pike,
Bethesda, Maryland 20014, USA)*

I shall largely speak of mice, but my thoughts are on man, on healing, on life and its evolution. Threatening life and evolution are the two deaths, death of the spirit and death of the body. Evolution, in terms of ancient wisdom, is the acquisition of access to the tree of life. This takes us back to the white first horse of the Apocalypse which with its rider set out to conquer the forces that threaten the spirit with death. Further in Revelation (ii.7) we note: 'To him who conquers I will grant to eat the tree of life, which is in the paradise of God' and further on (Rev. xxii.2): 'The leaves of the tree were for the healing of nations.'

This takes us to the fourth horse of the Apocalypse (Rev. vi.7): 'I saw . . . a pale horse, and its rider's name was Death, and Hades followed him; and they were given power over a fourth of the earth, to kill with the *sword* and with *famine* and with *pestilence* and by *wild beasts* of the earth' (italics mine). This second death has gradually become the predominant concern of modern medicine. And yet there is nothing in the earlier history of medicine, or in the precepts embodied in the Hippocratic Oath, that precludes medicine from being equally concerned with healing the spirit, and healing nations, as with healing the body. Perhaps we might do well to reflect upon another of John's transcriptions (Rev. ii.11): 'He who conquers shall not be hurt by the second death.'

Bodily Mortality

Let us first consider the second death (Table 1). The four mortality factors listed in Revelation have direct counterparts (with a division of one of them to form a total of five) in the ecology of animals in nature. I shall briefly treat each of

Table 1
The second death

As in Revelation vi.8	*Ecological expression*
(1) Sword	(1) Emigration
(2) Famine	(2*a*) Resource shortage
	(2*b*) Inclement weather (and fire and cataclysms of nature)
(3) Pestilence	(3) Disease
(4) Wild beasts	(4) Predation

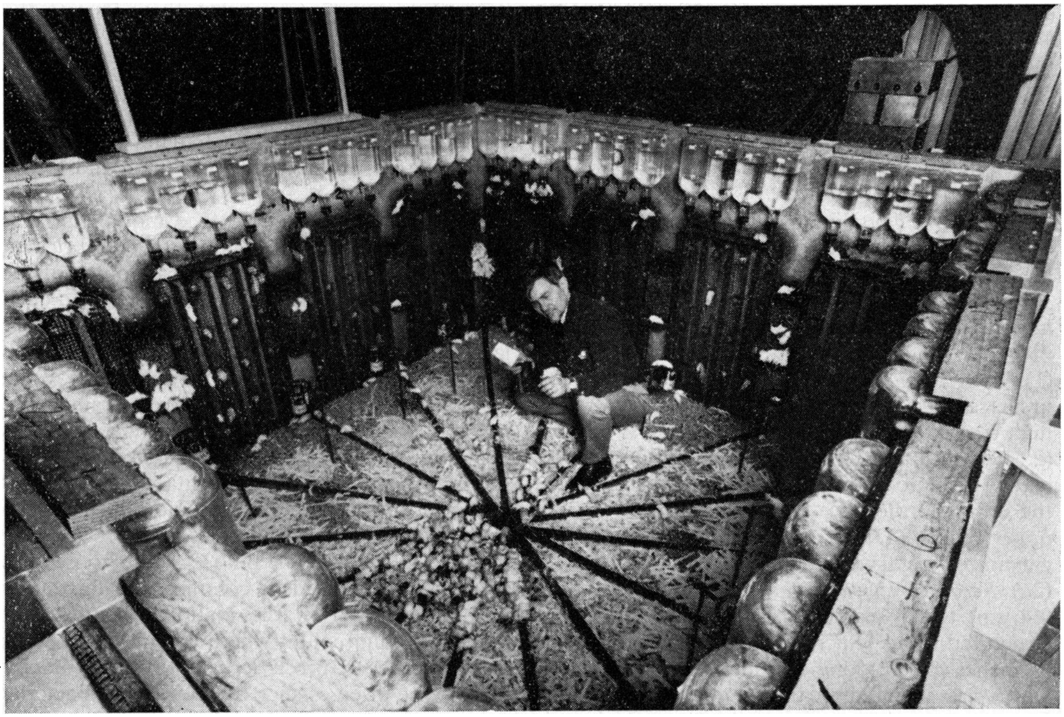

Fig 1 *Universe 25, February 10 1970, 681 days after colonization. Calhoun in universe with an exceptionally large aggregate of pooled withdrawn mice on the floor just across the centre of the floor from him. Note the aggregation of mice on some food hoppers in contrast to their near absence on others. This is the 'behavioural sink' phenomenon in which the learned need for proximity to others as a secondary reinforcer at a resource site gains dominance over the primary need, in this case food. Photo by Yoichi R Okamoto*

these five mortality factors, and then discuss the steps taken to eliminate, or drastically reduce, the impact of each in a Utopian environment constructed for mice.

(1) *Emigration:* Animals in the wild rarely die from the 'sword' directly; few are the deaths from intraspecific combat. Rather it is that individuals, who have failed in the more symbolic conflicts involved in gaining the right to remain in the locality of their birth or in more preferred habitats, take recourse to movement into peripheral unoccupied or suboptimal habitats. In strange and less favourable habitats the emigrés become more exposed to other mortality factors. Any removal of excess members from an established population, from the point of view of change in its numbers, represents mortality. In this sense emigration is a mortality factor.

(2*a*) *Resource shortage:* Classically food and water have received the focus of attention with respect to their reduction increasing the likelihood of death. Shortages of shelter, other environmental resources and associates lead to debilitation, and an unsatisfactoriness of habitat that culminate in death or failure to reproduce (species death).

(2*b*) *Inclement weather:* Every species of animal has developed a genetic adaptation to some particular range of external conditions which affect its physiology. Any conditions of wind, rain, humidity or temperature which exceed the usual limits of tolerance bring death immediately or increase the risk of death through debilitation. Beyond these more usual contributions to mortality, flood and fire represent cataclysmic changes that have widespread and more long-lasting effects on population numbers.

(3) *Disease:* Although most animals develop some capacity to tolerate the parasites, bacteria and viruses that invade their bodies, most species still remain subject to epidemic decimation in addition to a more normal attrition from disease. Abnormally high densities enhance the likelihood of spread of disease to epidemic proportions.

(4) *Predation:* Practically every species has, through evolution, had associated with it predators capable of killing some of its members.

Despite loss of members from these five kinds of mortality, most species persist over long periods, even those measured in geological time. To do so every such species has developed

capacities for reproduction requisite to compensate for losses from the normal impact of mortality factors other than ageing. I have omitted senescence as a mortality factor since rare is the animal who lives long enough in nature to reach a post-reproductive age without having succumbed to one of the above mortality factors.

A Mortality-inhibiting Environment for Mice
Some of the attributes of this environment have been discussed or figured elsewhere (Calhoun 1969, 1971, Wigotsky 1970). Here I shall describe how its design reduced mortality.

(1) *Emigration prevention:* A closed physical universe was formed by four 54 inch (1.37 m) high walls forming a square of side 101 inches (2.57 m). Although the walls were structured for use by mice to increase the effective use-area of the universe, the mice could not climb over the upper 17 inch (43 cm) unstructured portion of the galvanized metal walls.
(2*a*) *Resource supra-availability:* Each 25¼ inch (64 cm) linear segment of wall was identically structured. Four 3 inch (7.6 cm) diameter tunnels 34 inches (86 cm) long of ½ inch (12.5 mm) mesh wire were soldered vertically to the walls. The open lower end, just above the floor which was covered with ground corn cob, gave access to each tunnel. At 8 inch (20.3 cm) intervals above the floor in each tunnel four 1¼ inch (3.2 cm) openings through the tunnel mesh and the metal wall gave access to $8 \times 5 \times 4$ inch ($20.3 \times 12.7 \times 10.2$ cm) retreat nesting boxes. Fifteen mice could comfortably rest in a single nest box. Thus there were four four-unit walk-up one-room apartments in each cell. The cell is the replicated wall configuration, here being described, with an associated 640 sq. inch (0.356 m^2) of floor space. A wire mesh food hopper with a 6×10 inch (15×25 cm) surface was located in each of the 16 cells halfway up the wall and in contact with the right-hand tunnel of each set of four tunnels. Mice climbing across the outer surface of the tunnel gained access to the food hopper. Twenty-five mice could feed simultaneously on a hopper. By further climbing up the outside surface of the tunnels mice had access to a 4×18 inch (10×45 cm) platform above which four water bottles were suspended. Two mice could drink simultaneously at each bottle. An abundant supply of paper strips for nesting material was always available on the floor a few inches out from the bases of the tunnels. Considering the time required to eat and drink, access to food would not have been a limiting variable until a population of 9500 was reached, or 6144 for water. Considering that there were 256 nest retreat sites in the 16 cells one would not expect shelter to be a limiting factor until the population exceeded 3840. Due to the tendency of many animals to choose to crowd together in numbers in excess of 15 per nest site, at the peak population size of 2200 mice, 20% of all nest sites were usually unoccupied. Thus there was always opportunity for females to select an unoccupied space for rearing young if they so chose.
(2*b*) *Weather amelioration:* The mouse universe was located on the second floor of a prefabricated metal building. During the cooler months of the year ambient temperature was kept close to 68°F (20°C). During the warmer months of the year large exhaust fans kept ambient temperatures mostly within the 70–90°F (21–32°C) range of the outside environment. Being indoors, rain could not contribute to debilitation. Air movement was kept low, except when this favoured heat loss during periods of higher ambient temperature. No evidence was ever obtained to indicate that such weather conditions enhanced mortality.
(3) *Disease control:* The Balb C albino house mice (*Mus musculus*) used as colonizers in this study were obtained from the National Institutes of Health breeding colony where extreme precautions are followed to preclude establishment of epidemic type diseases such as salmonella. Bacterial culture taken at the highest density of the population indicated that such organisms were not a factor in our study. About every four to eight weeks the ground corn cob in all nest boxes and the floor was removed along with accumulated fæces.
(4) *Predation:* No predators were present.

Some mortality did occur throughout the history of the population we initiated in this 16 cell universe. Not until the mice became quite old did the mortality from ageing contribute significantly to removal of members from the population. On the basis of initial analyses, menopause in females comes at about 560 days of age. Although we have not yet determined the average life expectancy at weaning, I suspect that it is well past menopause. Large numbers of mice lived to 800 days of age, which is equivalent to 80 years of age for a human.

Explosive Initial Population Growth, the Resource Exploitation Phase B
Four pairs of 48-day-old Balb C strain house mice were introduced into the 16 cell universe on July 9 1968, after each mouse had been isolated for 21 days following weaning. There followed a period of 104 days (Phase A) before the first litters were born. These 104 days were marked by considerable social turmoil among these 8 mice until they became adjusted to each other and to their expanded surroundings. Following this

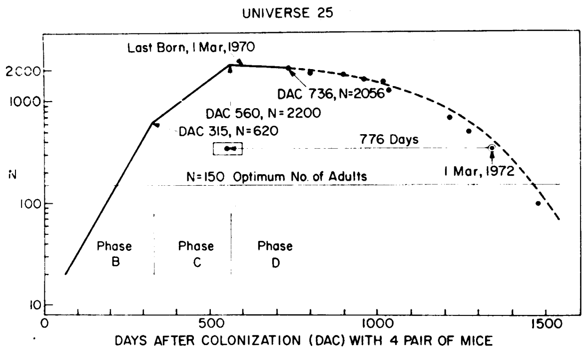

Fig 2 *History of population of mice in a closed Utopian universe. Broken line represents an estimate of numbers made about 700 days after colonization on the basis of observed mortality to that time. Observed points after Day 1000 are slightly lower than projected due to removal of about 150 mice for other studies. A final point was added to the graph for Day 1471 when the population had decreased to 100. At final editing of this paper on November 13, 1972 (Day 1588) the inexorable decline brought the population to 27 (23 females and 4 males, the youngest of which exceeded 987 days of age)*

adjustment and the birth of the first litters the population exhibited an exponential increase, with a doubling time of about 55 days (Fig 2). This progression of numbers was approximately 20, 40, 80, 160, 320, to 620 after nearly five doublings. I call this period of most rapid growth Phase B. At 620 weaned mice the rate of population growth abruptly decreased to a doubling time of approximately 145 days. Periodically through Phase B, young born into the universe reached sexual maturity and bore young, thus contributing to the compound interest rate of population growth.

Distribution of place of birth (Fig 3) of mice born during Phase B provides an insight into the social organization that developed. The square represents the wall of the pen, and the small black rectangles depict the locations of the food hoppers along its inner surface. Between each two hoppers there are four sets of walk-up apartments, each set containing four nest boxes accessible by a single tunnel. The total young born in each of the 64 sets of four nest boxes were tabulated for the period through the first survey after the termination of Phase B. These totals are shown in Fig 3 as open bars extending outward from the wall of the pen.

It may be seen that births tended to be concentrated in some sets of nest boxes, while others had few or none. This uneven distribution of births reflects a clustering of reproducing females into brood groups defined in Fig 3 by lines radiating toward the centre of the universe from the bases of nest boxes at the interface between each two adjoining brood groups. Total births per brood group are indicated between radial lines. These totals reflect two properties of a closed social system:

(1) *Bilateral symmetry:* The northeast brood group produced only 13 young in 252 days whereas the opposite southwest brood group produced over eight times as many, 111. Between these two extremes from the location of the peak producing brood group toward the least productive one, in both clockwise and counterclockwise directions, there is a decline in number of young born. This trend reflects the attempt by the members of the population to superimpose a more effective bilateral symmetry of organization

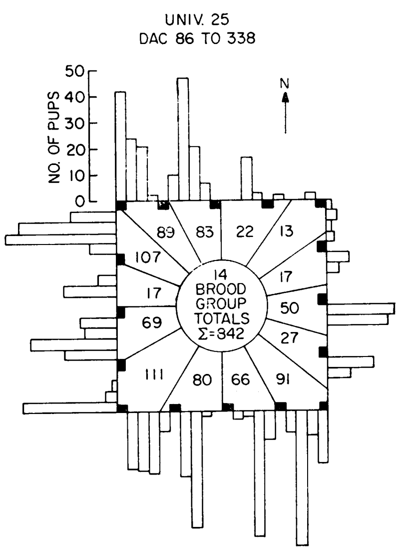

Fig 3 *Production of young between 86 and 338 days after colonization. Black rectangles represent location of food hoppers on inner surface of walls of the universe. Bar graph represents number of young born in each vertical set of four nest boxes*

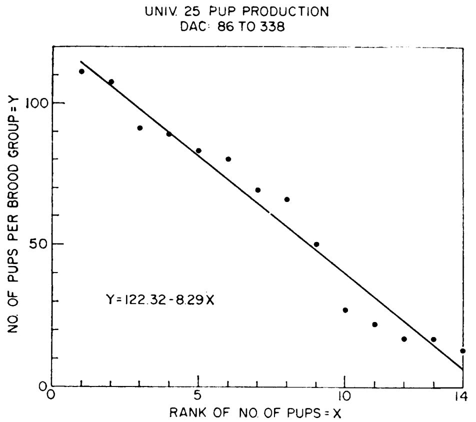

Fig 4 *Rank-frequency curve of production of young by brood groups. Number of young in a brood group reflects the degree of dominance of the territorial male associated with the brood group*

upon an environment that tends toward radial symmetry.

(2) *Hierarchy of groups:* Productivity of a group may be taken as an index of its social status. The fourteen brood groups may thus be ranked with rank No. 1 assigned to the group which produced 111 young, and rank No. 14 to the one which produced only 13 young. Plotting the number of young produced as a function of this ranking (Fig 4) reflects a remarkable hierarchical ordering within the total social system. This type of ordering is identical to that which results when we examine the degree of activity exhibited by the several males of an interacting group. The most dominant male is the most active one, and as social dominance declines so does the degree of activity. Such activity is termed 'social velocity' (Calhoun 1963, 1967, 1971). Our studies show that in a group of 14 males social velocity declines linearly with rank with approximately the same slope as in Fig 4. Each of the brood groups had associated with it a male which was territorially dominant within an area on the floor roughly coinciding with the sectors shown in Fig 3. All the ranges of these territorial males overlapped near the centre of the universe. The most dominant male was always associated with the brood group that produced the most young, and the degree of dominance of the other territorial males tended to be reflected by the productivity of females associated with them.

Both bilateral and hierarchical social organization during Phase B contributed to a maximum exploitation of resources that led to an explosive rate of increase of the population. At the end of this phase all the most desirable physical space was filled with organized social groups. These 14 social groups totalled 150 adults. On average each group contained over 10 individuals including a territorial male, associated males and females, and their juvenile and subadult progeny. At the end of Phase B there were 470 of these immature mice that had experienced good maternal care and early socialization. Thus there were over three times as many younger animals as the socially established older ones. This number is far greater than would have existed had the normal ecological mortality factors functioned.

Inhibited Secondary Population Growth, the Stagnation Phase C

Beginning at Day 315 after colonization and continuing for 245 more days, the population grew at a much slower rate, doubling only every 145 days rather than each 55 days as in Phase B. Let us examine the circumstances surrounding this decline in rate of population growth. In the normal course of events in a natural ecological setting somewhat more young survive to maturity than are necessary to replace their dying or senescent established associates. The excess that find no social niches emigrate. However, in my experimental universe there was no opportunity for emigration. As the unusually large number of young gained adulthood they had to remain, and they did contest for roles in the filled social system. Males who failed withdrew physically and psychologically; they became very inactive and aggregated in large pools near the centre of the floor of the universe. From this point on they no longer initiated interaction with their established associates, nor did their behaviour elicit attack by territorial males. Even so, they became characterized by many wounds and much scar tissue as a result of attacks by other withdrawn males. Return of 2 or more males, who had gone to eat and drink, marked an abrupt shift in the level of ambient stimuli for their quiescent associates. Resultant excitation often precipitated one of the resting males into an attack upon his other withdrawn associates who, having lost the capacity for fleeing, remained relatively immobile despite receiving vicious attacks. A mouse so attacked would at a later time become an attacker. Female counterparts of these withdrawn males tended to withdraw to higher level boxes that were less preferred by females with litters. Such females were not characterized by the violent aggression of the withdrawn males.

As a result of the extreme demands made on territorial males to reject maturing associates, their ability to continue territorial defence declined. Gradually the frequency of this involvement in territorial defence declined as did the area defended. This left nursing females more exposed to invasion of their nest sites. Normally nursing females in the presence of territorial

males exhibit little aggression. However, in response to invasion of nest sites and bases of ramps leading to them, the nursing females did become aggressive, essentially taking over the role of the territorial males. This aggression generalized to their own young who were attacked, wounded, and forced to leave home several days before normal weaning. During Phase C the incidence of conception declined, and resorption of fœtuses increased. Maternal behaviour also became disrupted. Young were often wounded in the delivery process. Females transported their young to several sites, during which process some were abandoned. Many litters of a young age on one survey disappeared before the next survey. Such abandoning of young following survey disturbance is a particularly sensitive index of dissolution of maternal behaviour. The combined effect of these several factors affecting reduced conception, increased fœtal mortality and increased preweaning mortality largely accounts for the abrupt decline in rate of population growth characterizing Phase C. For all practical purposes there had been a death of societal organization by the end of Phase C.

Decline of Population Size, the Death Phase D

Population increase abruptly ceased on Day 560 after colonization. A few mice born up until Day 600 survived past weaning. Between these times deaths just slightly exceeded births. Beyond the time of the last surviving birth on Day 600 the incidence of pregnancies declined very rapidly with no young surviving. Last conception was about Day 920. With the increase in rate of mortality accompanying senescence the population has continued to decline in numbers. By March 1 1972, the average age of survivors was 776 days, over 200 days beyond menopause. On June 22 1972, there were only 122 (22 male, 100 female) survivors. Projection of the prior few months of exponential decline in numbers indicates that the last surviving male will be dead on May 23 1973, 1780 days after colonization. The population will be, reproductively, definitely dead at that time, although such death was predicted by 700 days after colonization. This demise of a population contradicts prior knowledge which indicates that when a population declines to a few remnant groups, some individuals will reinitiate its growth.

Turning back to the end of Phase C, the seeds for eventual destruction may already be seen to have been sown. By midway in Phase C essentially all young were prematurely rejected by their mothers. They started independent life without having developed adequate affective bonds. Then as they moved out into an already dense population many attempts to engage in social interaction were mechanically disrupted by passage of other mice. Lastly, I have shown (Calhoun 1963) that in proportion to the extent that the group size exceeds the optimum, maximizing gratification from such interactions necessitates a decrease in the intensity and duration of such behaviours. This fragments otherwise more complex behaviours. As a result of these three processes (failure to develop early social bonding, mechanical interference with developing social behaviours and fragmentation of behaviours) maturation of the more complex social behaviours such as those involved in courtship, maternality and aggression failed. For females a clear example may be taken from a 2 cell universe studied in parallel with the 16 cell one detailed here. The members of this population were killed 300 days after the inflection point of the shift from Phase C to Phase D. Among these were 148 females born within the last 50 days before the end of Phase C. At autopsy at a median age of 334 days only 18% had ever conceived (i.e. no placental scars in the uteri of 82% of the females) and only 2% were pregnant (each of these 3 females had only one embryo as contrasted to the more normal 5 or more). By this age most females in a normal population would have had five or more litters, most of them successfully reared.

Male counterparts to these non-reproducing females we soon dubbed the 'beautiful ones'. They never engaged in sexual approaches toward females, and they never engaged in fighting, and so they had no wound or scar tissue. Thus their pelage remained in excellent condition. Their behavioural repertoire became largely confined to eating, drinking, sleeping and grooming, none of which carried any social implications beyond that represented by contiguity of bodies.

Most of the last half of the population born in the 16 cell universe were fully or largely like these non-reproducing females and these 'beautiful ones' (males). As their formerly more competent predecessors gradually became senescent, their already disrupted capacity for reproduction terminated. At this time only the 'beautiful one' category of males, and their counterpart females, remained at an age normally compatible with reproduction, but they had long since failed to develop this capacity.

My colleague, Dr Halsey Marsden (1972), conducted several studies during the mid-third of Phase D in which he placed small groups of mice out of these crowded populations into new universes at very low densities. All groups exhibited nearly total loss of capacity for developing a structured society or for engaging in the full repertoire of reproductive behaviours. Even placing them with adequate sex partners of the

opposite sex, that had matured in uncrowded conditions, also gave very little indication of retention of any adequate reproductive behaviour.

Conclusion

The results obtained in this study should be obtained when customary causes of mortality become markedly reduced in any species of mammal whose members form social groups. Reduction of bodily death (i.e. 'the second death') culminates in survival of an excessive number of individuals that have developed the potentiality for occupying the social roles characteristic of the species. Within a few generations all such roles in all physical space available to the species are filled. At this time, the continuing high survival of many individuals to sexual and behavioural maturity culminates in the presence of many young adults capable of involvement in appropriate species-specific activities. However, there are few opportunities for fulfilling these potentialities. In seeking such fulfilment they compete for social role occupancy with the older established members of the community. This competition is so severe that it simultaneously leads to the nearly total breakdown of all normal behaviour by both the contestors and the established adults of both sexes. Normal social organization (i.e. 'the establishment') breaks down, it 'dies'.

Young born during such social dissolution are rejected by their mothers and other adult associates. This early failure of social bonding becomes compounded by interruption of action cycles due to the mechanical interference resulting from the high contact rate among individuals living in a high density population. High contact rate further fragments behaviour as a result of the stochastics of social interactions which demand that, in order to maximize gratification from social interaction, intensity and duration of social interaction must be reduced in proportion to the degree that the group size exceeds the optimum. Autistic-like creatures, capable only of the most simple behaviours compatible with physiological survival, emerge out of this process. Their spirit has died ('the first death'). They are no longer capable of executing the more complex behaviours compatible with species survival. The species in such settings die.

For an animal so simple as a mouse, the most complex behaviours involve the interrelated set of courtship, maternal care, territorial defence and hierarchical intragroup and intergroup social organization. When behaviours related to these functions fail to mature, there is no development of social organization and no reproduction. As in the case of my study reported above, all members of the population will age and eventually die. The species will die out.

For an animal so complex as man, there is no logical reason why a comparable sequence of events should not also lead to species extinction. If opportunities for role fulfilment fall far short of the demand by those capable of filling roles, and having expectancies to do so, only violence and disruption of social organization can follow. Individuals born under these circumstances will be so out of touch with reality as to be incapable even of alienation. Their most complex behaviours will become fragmented. Acquisition, creation and utilization of ideas appropriate for life in a post-industrial cultural-conceptual-technological society will have been blocked. Just as biological generativity in the mouse involves this species' most complex behaviours, so does ideational generativity for man. Loss of these respective complex behaviours means death of the species.

Mortality, bodily death = the second death
Drastic reduction of mortality
=death of the second death
=death squared
$=(\text{death})^2$
$(\text{Death})^2$ leads to dissolution of social organization
=death of the establishment
Death of the establishment leads to spiritual death
=loss of capacity to engage in behaviours essential to species survival
=the first death
Therefore:
$(\text{Death})^2 =$ the first death.

Happy is the man who finds wisdom,
and the man who gains understanding.
Wisdom is a tree of life to those who
lay hold of her.
All her paths lead to peace.
(Proverbs iii.13, 18 and 17, rearranged)

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DISCUSSION

The Chairman thought Dr Calhoun had not mentioned pollution and asked what remains the animals left and how these affected the situation?

Dr Calhoun said that they (the investigators) were not very sanitary in their husbandry, if that was the kind of pollution inferred. The environment was cleaned, most fæces and soiled bedding removed, every six weeks or two months, but nothing was ever sterilized. He did not consider this necessary in such a closed system and the mice had better survival than in most laboratory colonies. Dead bodies were eventually removed for examinations, but the major pollution was the excess of living bodies; this was the essential factor. The pollution was social in that there were too many interacting elements, exceeding the social system's capacity for incorporation of new individuals. Capacities were genetically determined and situationally modified.

The Chairman thought the point had been made very clearly, but there must be a pollution factor. There were the remains, fæces, urine and dead bodies. Those must surely be a factor.

Dr Calhoun thought these were minor factors. They needed to maintain a situation in which there was not continuous waste accumulation, but beyond that the environment mirrored certain normal, external ecological settings.

Dr John F Stokes (*London*) said he was interested in Dr Calhoun's diagram illustrating pupping rates, which showed much greater fertility in the south and west than in the north and east. If he had understood the construction of Dr Calhoun's 'universe' correctly, there were no external indications which could tell the mice in which direction they faced (though there was an arrow pointing north on the diagram). He enquired whether Dr Calhoun thought that other influences might determine the uneven distribution of pups.

Dr Calhoun replied that it was his present conviction that the social system of mice in Universe 25 would have developed a bilateral symmetry of organization whether or not some external cues might have influenced the particular direction that the social axis assumed. Four other smaller mouse populations had not been examined for geographical orientation. Other factors such as air flow could have had some influence, but he thought the uneven distribution was a chance phenomenon which once established maintained itself through social processes.

The Chairman observed that Dr Calhoun had stated that the dominant males were more active. He asked how this had been measured.

Dr Calhoun said that animals were individually colour marked and that specific locations in the environment were coded. Visual observations of the degree of movement of individuals and in what place were correlated with data on social interactions. They had taken about a million observations on the set of populations, of which Universe 25 was the largest and had been followed for the longest period of time. It had been a long-term study and they were in the process of structuring their data on magnetic tape for detailed analysis.

Professor R A Weale (*Institute of Ophthalmology, London*) said that the appearance of Dr Calhoun's mice resulting from the colour coding he used might affect their behaviour even though they had no colour vision.

Dr Calhoun replied that this was a frequent question, that there were preliminary indications of some effect but the question could not really be answered until statistical analyses were available. Whether these effects were visual or olfactory could not be determined but in any case the mice were capable of recognizing each other without markings. Movements and body posture conveyed a great deal of information and he thought these factors were far more important than colour.

Professor Mellanby said Dr Calhoun had suggested that by 1984 man was going to be as crowded as his mice and that this would have disastrous effects. Experiments had been going on for a long time with man. Man was not uniformly distributed. He lived in some communities just as crowded as Dr Calhoun's mice. Professor Mellanby had been very familiar with populations in parts of London forty years ago which were restricted communities. People seldom moved out of them. Until the children were taken to camps for holidays they had seldom been more than a quarter of a mile from their homes. They were living amidst extreme crowding and bred very successfully. Therefore, was it not possible to get an answer to this for human beings by examining such communities? Did crowded, enclosed communities behave like the mice? Or did this occur most obviously in those communities which had about the lowest population density in Sweden or the United States?

Dr Calhoun replied that 1984 was not the year in which ultimate density would be attained, but a date beyond which the opportunity for decision making and designing to avoid population catastrophe might be quickly lost. He stated, in any case, that density *per se* was not the major factor, that rate and quality of social interaction were paramount issues. Basic to his thesis was that despite the thousandfold increase in human numbers since the beginning of culture, some forty to fifty thousand years ago, there had been no change in effective density. The reason for this, alluded to by Professor Young, was that man had discovered a new kind of space, conceptual space, which enabled man to utilize ideas in order to mine resources and guide social relations. However, there was a breaking point for this process, at which time physical density might overwhelm man's ability to utilize conceptual space in order to cope with increasing numbers and it was that breaking point which we might be rapidly approaching. The fact that reproduction could be affected by density had been dealt with by Dr Thompson in Indianapolis (Thompson 1969). An older study for Scotland (Kincaid 1965) had shown that stillbirths and other parameters were density

related. However, in terms of conceptual space, it might be the *necessity for limitations* to growth which might be the more difficult conceptual area for man to deal with. In that case a further increase in birth rate might be expected past the breaking point (Galle *et al.* 1972).

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The Chairman interrupted Dr Calhoun and said that he ought to be careful about this. He had been discussing mice, and the Chairman agreed with Professor Mellanby that there were some very strong contraindications. Hong Kong, for example, was a most marvellous population of people living under much higher densities than in east London. He thought the inhabitants to be impressively happy as far as one could see.

Dr Calhoun thought this to be a major trap. The essential core of man was to remain under tension. What happened in the mice was this: He called the males the 'beautiful ones'. Those at the end had a kind of autistic life. They could function under normal routine conditions but beyond this the major powers of the species were lost. He did not know what happened in Hong Kong. He had been in Calcutta and was frightened by it. His interpretation of what was happening there might be happening in Amsterdam and other places now. He thought mankind was on a knife-edge which could shift in a couple of directions. One behavioural shift on the human side could be comparable to 'beautiful one' mice: individuals capable of the routine of life, but with loss of creativity and an inability to live under challenge.

Mr Selwyn Taylor (*London*) asked Dr Calhoun if he had made any measurements of the endocrine parameters in his mice in the declining part of the population curve?

Dr Calhoun replied that Dr Julius Axelrod and Dr Larry Ng and their associates had measured catecholamine synthesizing enzymes in brain and adrenal glands in mice selected (by Dr Calhoun, Dr Marsden and their associates) to represent specific behavioural states existing during the declining crowded populations. It (neuroendocrinology) was not his field but, in general, the biochemical picture suggested a higher degree of physiological stress in 'socially withdrawn' mice as opposed to aggressive territorial mice. An intriguing finding related to a third group of mice, the 'beautiful ones', mice in excellent physical condition but mice which did not engage in social interaction. Their catecholamine metabolism was comparable to the territorial animals. They were physically healthy but never attempted to cope with the social situation. Rather than socially withdrawing from the system, the implication was that they never attempted to enter it. All of these various types of mice evolved in the crowded environment but because of differing roles, or rather lack of social roles or rejection from attempted roles, their behavioural and biochemical profiles were quite different.

The Chairman asked about the steroids.

Dr Calhoun said that a more comprehensive picture of the physiology was not obtained. Such a co-ordinated effort had to be planned from the beginning. The real dilemma was the removal of sufficient numbers of animals with known histories at critical points in population growth. Removal of large numbers of animals at any point in a population's history presented the risk of disturbing the later history. The only effective approach would be to run a large number of populations and terminate them at critical periods. The labour problem was tremendous. This was not normal science, a balanced experiment. It was observation and reconstruction of a process; it was historical.

Dr James P Henry (*University of Southern California*) said that for the past ten years his group had been following up on Dr Calhoun's approach of working with socially interacting, freely breeding groups of rodents. They had used smaller colonies of 17 to 50 CBA mice and had studied normal and socially deprived animals using intercommunicating systems of standard boxes. Role behaviour was monitored by a magnetic tagging method (Ely *et al.* 1972). In the socially deprived groups persistent fighting and social disorder had been associated with a slowly developing elevation of the adrenal medullary catecholamine-synthesizing enzymes, tyrosine hydroxylase and phenylethanolamine N-methyltransferase (Henry, Stephens *et al.* 1971). There had been a sustained systolic arterial hypertension. After several months this had become fixed, despite removal of the stimulus (Henry *et al.* 1967). In animals which had experienced six months or more of this social stimulation there had been a gross increase in the incidence and severity of aortic and intramural coronary vascular arteriosclerosis, of glomerular mesangial changes, and of myocardial fibrosis and chronic interstitial nephritis (Henry, Ely *et al.* 1971).

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Dr John Burkinshaw (*London*) wondered whether throughout his experiment Dr Calhoun had observed anything among the mice which could be interpreted as a mutation.

Dr Calhoun felt that there probably was some mutation. Mice which continually circled, about a dozen, had been noted, but these might have been 'vestibular' mice and a result of an infection, not mutation. Even if mutation rates were known, the first generation would have been very much like the last. So the real conclusion was that tremendous behavioural differentiation could occur as a result of social environmental influences even given a high degree of genetic homozygosity.